Claims 18-20 have been rejected under §112. On pages 3-4, the Office Action states that the specification does not provide a way to make and/or use the invention. Applicants respectfully disagree with the rejection.

There are three types of reporter (marker) gene products that are expressed from reporter genes. The reporter gene/protein systems include:

a) Intracellular gene products such as luciferase or chloramphenicol acetyl transferase (CAT). Typically, they are enzymes whose enzymatic activity can be easily measured.
b) Intracellular gene products such as E. coli ß-galactosidase or green fluorescent protein (GFP). On the basis of the intensity of cellular staining, these reporter gene products also yield qualitative information concerning the amount of foreign protein produced per cell.
c) Secreted gene products such as human growth hormone are useful for determining the amount of a secreted protein that a gene transfer procedure can produce.

Applicants have disclosed gene expression from luciferase and beta-galactosidase reporter genes in cardiac tissue. Since polynucleotides are all structurally identical, sequence differences among polynucleotides should not produce different or negative effects on delivery and expression for other gene sequences. The levels achieved indicate a reasonable expectation of any gene expression to a person having skill in the art of methods of delivery.

In the field of gene delivery, it is accepted that the level of expression of a given gene can be regulated by the choice of promoter and other regulatory sequences. The level of expression required depends on each application. However, as cited in the Office Action on page 4, Verma et al. and Anderson et al. indicate that the critical step in gene therapy is transfer of the nucleic acid into the target cells. The target cells in Applicants' specification are cardiac tissue cells, more specifically: heart muscle cells to which genes were delivered and expressed efficiently. By analogy, a gene can reasonably be expected to be delivered and expressed using the described process.

Therefore, Applicants believe they have reasonably described and enabled their invention. Applicants respectfully request that the §112 be removed based upon the material in the specification.

Objection to the Specification under 35 U.S.C. 112:

Claims 1-20 have been rejected under §112 second paragraph for being indefinite.

On page 4, claim 1 is rejected for the use of "cardiac tissue." The claim has been amended to substitute "heart muscle" to obviate the rejection. Support for the amendment may be found in the specification on page 8, line 38 and throughout.

On page 5, claim 1 is rejected for reciting the term "vessel." Claim 1 has been amended to substitute the term "blood vessel." Support for the amendment may be found in the specification on page 7, line 20 and throughout.

Claims 3 and 8 are rejected for using the term "inserting" because it has no antecedent basis. However, the term has antecedent basis in the specification such as on page 10, line 14. Therefore, applicants request that the rejection be removed.

Claims 6, 11, 14 and 17 are objected to for reciting the term "viruses" as a nucleic acid. The claims have been amended to include the modifier "nucleic acid contained in viruses" as suggested in the Office Action. Support for the amendment may be found in the specification on page 15, line 6.

Claim 7 is considered vague and indefinite by reciting "nucleic acid modifies expression of cellular material." Claim 7 has been amended to the recitation "nucleic acid modifies expression in a cell." The claim now recites a definite structure.

Claim 12 is rejected for reciting "changing a predetermined volume of nucleic acid" as being vague and confusing. Claim 12 has been amended to recite "injecting a predetermined volume of nucleic acid." The recitation uses terminology from prior claims and each term is clearly related to the claim from which it depends.

Claim 18 is stated to be incomplete because no process steps indicate therapy. Applicants have amended claim 18 to include a therapy step to obviate the objection. Support for the amendment may be found in the specification on page 14, line 23 and throughout.

Rejection of claims under 35 U.S.C. 102:

Claims 1-17 are rejected under §102(a) as being anticipated by Hajjar et al., Leclerc et al. Claims 1-20 are rejected under §102(a) as being anticipated by Isner et al. and Mann et al. Applicants have amended independent claim 1 to obviate the rejection.

Claim 1 has been amended to replace "cardiac tissue" with "heart muscle cell." Hajjar et al., Leclerc et al., and Isner et al. all disclose delivery of nucleic acid to endothelial cells. In contrast, Applicants disclose a process to deliver a nucleic acid to heart muscle cells, a significant difference which is not disclosed or taught by the prior art cited.

Mann et al. disclose a method of delivering nucleic acid to a heart that is encapsulated by a "sealed enclosure" device to retain and put pressure on the nucleic acid. Applicants' claimed process does not require such a device and is therefore distinguishable over the cited prior art.

Rejection of claims under 35 U.S.C. 103:

Claims 1-20 are rejected under §103(a) as being obvious over Mann et al. and Morishita et al. Applicants respectfully disagree.

As discussed in the section above, Mann et al. explicitly requires a sealed enclosure around the targeted organ to obtain transfection and expression. In addition, Morishita et al. discloses *in vitro* methods of transfection. Conversely, Applicants' process does not require a sealed enclosure nor is it performed *in vitro*. It is unlikely that a person having skill in the art would combine the two references to obtain an *in vivo* process of delivery and expression not requiring a sealed enclosure.

The Examiner's objections and rejections are now believed to be overcome by this response to the Office Action. In view of Applicants' amendments and discussion, it is submitted that claims 1-20 should be allowable and Applicants respectfully requests an early notice to such effect.

Respectfully submitted,

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I hereby certify that this correspondence is being facsimile transmitted to Robert Hill at the United States Patent and Trademark Office, Fax No.(703)305-7230 on December 12, 2000.

Signature 12/12/00
Date